

Abbreviation shRNA construct	Rel. rate of prion propagation			Gene silencing	
	FC	SD	t-test	% kd	SD
<i>shRNA-Galt.1</i>	1.60	0.32	2.2×10^{-3}	42	20
<i>shRNA-Galt.2</i>	0.91	0.28	3.9×10^{-1}	22	21
<i>shRNA-Galt.3</i>	1.18	0.20	1.7×10^{-1}	14	11
<i>shRNA-Galt.4</i>	1.82	0.50	2.5×10^{-5}	41	17
<i>shRNA-Galt.5</i>	0.45	0.26	4.2×10^{-3}	64	13
<i>shRNA-Galt.6</i>	0.88	0.20	2.9×10^{-2}	28	26
<i>shRNA-Iqgap2.1</i>	1.29	0.14	3.8×10^{-2}	24	19
<i>shRNA-Iqgap2.2</i>	1.44	0.36	1.2×10^{-2}	33	9
<i>shRNA-Iqgap2.3</i>	0.99	0.26	9.5×10^{-1}	23	8
<i>shRNA-Iqgap2.4</i>	5.65	1.07	1.3×10^{-17}	55	27
<i>shRNA-Iqgap2.5</i>	0.92	0.26	3.0×10^{-1}	38	18
<i>shRNA-Iqgap2.6</i>	0.81	0.24	2.1×10^{-1}	32	9
<i>shRNA-Slc26a4.1</i>	1.03	0.38	8.3×10^{-1}	88	13
<i>shRNA-Slc26a4.2</i>	1.25	0.58	1.5×10^{-1}	69	34
<i>shRNA-Slc26a4.3</i>	1.48	0.48	1.9×10^{-2}	83	13
<i>shRNA-Slc26a4.4</i>	0.93	0.55	6.7×10^{-1}	78	14
<i>shRNA-Slc26a4.5</i>	1.23	0.71	3.4×10^{-1}	89	23
<i>shRNA-Chga.1</i>	4.41	1.36	9.8×10^{-7}	58	12
<i>shRNA-Chga.2</i>	4.30	0.80	4.3×10^{-8}	55	21
<i>shRNA-Chga.3</i>	1.12	0.43	5.2×10^{-1}	32	25
<i>shRNA-Chga.4</i>	1.30	0.63	8.2×10^{-1}	23	7
<i>shRNA-Chga.5</i>	1.14	0.57	6.5×10^{-1}	18	24
<i>shRNA-Id4.1</i>	0.87	0.27	7.9×10^{-2}	46	4
<i>shRNA-Id4.2</i>	1.46	0.37	3.8×10^{-2}	43	4
<i>shRNA-Id4.3</i>	1.12	0.39	3.7×10^{-1}	39	2
<i>shRNA-Id4.4</i>	0.75	0.31	1.2×10^{-2}	72	8
<i>shRNA-Id4.5</i>	0.80	0.44	2.0×10^{-1}	51	14
<i>shRNA-Id4.7</i>	0.95	0.20	5.8×10^{-1}	46	19
<i>shRNA-Id4.8</i>	0.88	0.22	2.8×10^{-1}	48	31
<i>shRNA-IL11ra1.1</i>	2.46	0.92	5.6×10^{-5}	54	8
<i>shRNA-IL11ra1.2</i>	3.15	0.79	2.6×10^{-7}	84	18
<i>shRNA-IL11ra1.3</i>	2.24	0.98	3.4×10^{-3}	50	30
<i>shRNA-IL11ra1.4</i>	0.93	0.26	5.2×10^{-1}	12	9
<i>shRNA-IL11ra1.5</i>	1.14	0.32	7.2×10^{-1}	31	8
<i>shRNA-IL11ra1.6</i>	1.09	0.49	8.7×10^{-1}	19	12
<i>shRNA-Lrrn4.1</i>	1.03	0.53	9.0×10^{-1}	73	13
<i>shRNA-Lrrn4.2</i>	0.75	0.27	2.7×10^{-2}	77	17
<i>shRNA-Lrrn4.3</i>	0.54	0.12	7.9×10^{-3}	81	16
<i>shRNA-Lrrn4.4</i>	0.68	0.18	1.1×10^{-1}	85	4
<i>shRNA-Fn1.1</i>	1.81	0.45	5.6×10^{-5}	72	12
<i>shRNA-Fn1.2</i>	3.15	0.66	9.9×10^{-5}	89	17
<i>shRNA-Fn1.3</i>	1.74	0.44	8.6×10^{-4}	70	14
<i>shRNA-Fn1.5</i>	1.53	0.83	5.4×10^{-1}	61	13

<i>shRNA-Fn1.6</i>	3.39	0.42	3.5×10^{-10}	87	23
<i>shRNA-Micalcl.1</i>	2.85	0.59	5.9×10^{-9}	95	15
<i>shRNA-Micalcl.2</i>	1.89	0.37	2.8×10^{-4}	87	33
<i>shRNA-Micalcl.3</i>	2.47	0.16	9.2×10^{-6}	83	16
<i>shRNA-Micalcl.4</i>	1.66	0.33	1.7×10^{-2}	86	4
<i>shRNA-Rgs4.1</i>	2.54	0.49	4.3×10^{-7}	75	19
<i>shRNA-Rgs4.2</i>	2.61	0.42	8.3×10^{-4}	69	12
<i>shRNA-Rgs4.3</i>	2.01	0.42	5.7×10^{-5}	77	14
<i>shRNA-Rgs4.4</i>	1.90	0.43	7.6×10^{-4}	55	22
<i>shRNA-Rgs4.5</i>	3.44	0.99	1.5×10^{-7}	80	16
<i>shRNA-Rgs4.6</i>	1.82	0.31	7.6×10^{-4}	61	3
<i>shRNA-Rgs4.7</i>	2.91	0.27	1.7×10^{-8}	65	17
<i>shRNA-Papss2.1</i>	2.32	0.13	1.6×10^{-9}	48	9
<i>shRNA-Papss2.2</i>	2.36	0.30	4.7×10^{-9}	70	17
<i>shRNA-Papss2.3</i>	1.23	0.43	2.6×10^{-1}	21	13
<i>shRNA-Papss2.4</i>	1.23	0.16	7.5×10^{-2}	16	15
<i>shRNA-Igsf5.1</i>	0.87	0.33	4.3×10^{-1}	36	4
<i>shRNA-Igsf5.2</i>	1.42	0.41	6.5×10^{-2}	2	1
<i>shRNA-Igsf5.3</i>	1.13	0.63	5.3×10^{-1}	34	4
<i>shRNA-Igsf5.4</i>	0.94	0.28	7.5×10^{-1}	68	5
<i>shRNA-Bambi.1</i>	0.92	0.31	5.6×10^{-1}	75	6
<i>shRNA-Bambi.2</i>	1.19	0.23	1.4×10^{-1}	65	10
<i>shRNA-Fst.1</i>	0.97	0.39	8.0×10^{-1}	24	6
<i>shRNA-Fst.3</i>	1.15	0.08	1.6×10^{-1}	28	14
<i>shRNA-Fst.4</i>	0.69	0.36	2.6×10^{-2}	41	20
<i>shRNA-Fst.5</i>	0.98	0.09	8.1×10^{-1}	13	6
<i>shRNA-Fst.6</i>	1.07	0.34	5.4×10^{-1}	81	8
<i>shRNA-Dlc1.1</i>	0.73	0.13	4.9×10^{-2}	41	12
<i>shRNA-Dlc1.2</i>	1.34	0.27	2.0×10^{-2}	73	4
<i>shRNA-Dlc1.3</i>	1.03	0.08	5.0×10^{-1}	61	17
<i>shRNA-Itga8.1</i>	2.70	0.12	2.8×10^{-9}	85	13
<i>shRNA-Itga8.2</i>	0.89	0.26	5.0×10^{-1}	49	21

Supplementary Table S6: Validation of susceptibility gene candidates by gene silencing.

Revertant R7 cells transiently expressing shRNA against distinct gene candidates using the bicistronic vector pGIPZ were enriched for highly GFP-fluorescent cells and subsequently infected with RML mouse prions at a dilution of 2×10^{-5} . The rates of prion propagation were determined by SCA and normalized against cells transfected with non-silencing control vectors (NSC GIPZ). Relative rates of prion propagation expressed as fold change (FC) to controls (NSC) $\pm$ SD for at least three independent experiments are shown. The level of gene knockdown (% kd) was determined as described in Methods.